24. (New) The method of Claim 14, wherein the presence of a cytidine at thymine position 11 of SEQ ID NO: 5 is indicative of a greater likelihood of the individual having a cardiovascular disease.

C6 cont.

REMARKS

Amendments to the Claims

Claims 9-12, 14, and 17-20 have been amended to further and more particularly define that which Applicants regard as their invention, and new Claims 21-24 have been added.

Support for amendments to the claims is found throughout the specification. For example, page 36 ('Table 2') describes the polymorphisms of the invention, in particular, SEQ ID NO: 5, and clearly indicates that position 11 is the polymorphic site of SEQ ID NO: 5. No new matter has been added. Entry of these amendments and new Claims is respectfully requested.

Rejection of Claims 9-20 Under 35 U.S.C. §112, Second Paragraph

Claims 9-20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

The Examiner rejects Claims 9, 12, 14, 17 and 19 stating that the phrase "the polymorphic site" lacks antecedent basis. The Examiner further states that, with respect to Claims 9, 12, 14, 17 and 19, the term "the polymorphic site of SEQ ID NO: 5" is vague and indefinite because it is not clear which nucleotide of SEQ ID NO: 5 is the polymorphic site.

Applicants point out that, as shown in Table 2 on page 36 of the specification and in the Sequence Listing, the polymorphic site of SEQ ID NO: 5 is clearly indicated as nucleotide position 11 (the only polymorphic site shown in the sequence). Nonetheless, to expedite

prosecution, the Claims have been amended to delete this phrase. Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 9-20 Under 35 U.S.C. §102(b)

Claims 9-20 are rejected under 35 U.S.C. §102(b) as being anticipated by Helbecque *et al.* (1997, *Arterioscler. Thromb. Vasc. Biol.*, 17:2759-2764; Reference AZ). The Examiner indicates that Helbecque *et al.* teach the association of a VLDL-R polymorphism and plasma lipoprotein levels.

Applicants respectfully traverse this rejection. In order for a reference to anticipate a claim under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. (MPEP 706.02). Applicants point out that nowhere do Helbecque *et al.* teach the specific polymorphism of SEQ ID NO: 5, at nucleotide position 11, as shown in Table 2 and in the Sequence listing. Helbecque *et al.* only describe a specific type of genetic anomaly, *i.e.*, variable numbers of triplet repeats that is 19 bp upstream of the initiation codon. Moreover, the teachings of Helbecque *et al.* do ***not*** indicate that ***all*** occurrences of the triplet repeat represent polymorphic variation. Applicants note that the nucleotide position of the variable number of 'CGG' repeats taught by Helbecque *et al.* does not correspond to nucleotide position 11 of SEQ ID NO: 5. Despite the Examiner's observation that indeed SEQ ID NO: 5 contains a 'CGG' sequence, Applicants note that the 'CGG' sequence of SEQ ID NO: 5 has not been described as a polymorphic site in the specification, is not claimed as a polymorphic site, does not contain the polymorphic site located at nucleotide position 11 of SEQ ID NO: 5. Therefore, because the teachings of Helbecque *et al.* do not disclose the polymorphic site of SEQ ID NO: 5, they do not anticipate the methods of Applicants' claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

9. (Twice Amended) A method of analyzing a nucleic acid sample for polymorphisms associated with cardiovascular disease, comprising the steps of:

(a) obtaining a nucleic acid sample from one or more individuals, and

(b) determining the nucleotide occupying nucleotide position 11 [the polymorphic site] of SEQ ID NO: 5.

10. (Twice Amended) A method according to Claim 9, wherein a plurality of nucleic acid samples is obtained from a plurality of individuals, and the nucleotide occupying [one or more polymorphic sites] nucleotide position 11 of SEQ ID NO: 5 is determined in each of the individuals.

11. (Amended) A method according to Claim 9, further comprising testing each individual for the presence of a disease phenotype and correlating the presence of the disease phenotype with the nucleotide present at nucleotide position 11 of SEQ ID NO: 5 [one or more polymorphic sites].

12. (Twice Amended) A method for predicting the likelihood that an individual will have a cardiovascular disease, comprising the steps of:

(a) obtaining a nucleic acid sample from an individual to be assessed; and

(b) determining the nucleotide present at nucleotide position 11 of SEQ ID NO: 5 [a polymorphic site of] for one or more nucleic acid molecules having a nucleotide sequence comprising SEQ ID NO: 5,

wherein the presence of a nucleotide associated with a lower likelihood of having a cardiovascular disease indicates that the individual has a lower likelihood of having a

cardiovascular disease than if another nucleotide were [was] present at nucleotide position 11 of SEQ ID NO: 5 [the polymorphic site].

14. (Twice Amended) A method for predicting the likelihood that an individual will have a cardiovascular disease, comprising the steps of:

(a) obtaining a nucleic acid sample from an individual to be assessed; and

(b) determining the nucleotide present at nucleotide position 11 of SEQ ID NO: 5 [a polymorphic site of] for one or more nucleic acid molecules having a nucleotide sequence comprising SEQ ID NO: 5,

wherein the presence of a nucleotide associated with a greater likelihood of having a cardiovascular disease indicates that the individual has a greater likelihood of having a cardiovascular disease than if another nucleotide were [was] present at nucleotide position 11 of SEQ ID NO: 5 [the polymorphic site].

17. (Amended) A method for predicting the likelihood that an individual will have coronary heart disease, comprising the steps of:

(a) obtaining a nucleic acid sample from an individual to be assessed; and

(b) determining the nucleotide present at nucleotide position 11 of SEQ ID NO: 5 [a polymorphic site of] for one or more nucleic acid molecules having a nucleotide sequence comprising SEQ ID NO: 5,

wherein the presence of a nucleotide associated with a lower likelihood of having coronary heart disease indicates that the individual has a lower likelihood of having coronary heart [a cardiovascular] disease than if another nucleotide were [was] present at nucleotide position 11 of SEQ ID NO: 5 [the polymorphic site].

18. (Amended) The method of Claim 17, wherein the presence of a cytidine [is present] at [the polymorphic site] nucleotide position 11of SEQ ID NO: 5 is indicative of a lower likelihood of the individual's having coronary heart disease.

19. (Amended) A method for predicting the likelihood that an individual will have coronary heart disease, comprising the steps of:

(a) obtaining a nucleic acid sample from an individual to be assessed; and

(b) determining the nucleotide present at nucleotide position 11 of SEQ ID NO: 5 [a polymorphic site of] for one or more nucleic acid molecules having a nucleotide sequence comprising SEQ ID NO: 5,

wherein the presence of a nucleotide associated with a greater likelihood of having coronary heart disease indicates that the individual has a greater likelihood of having coronary heart [a cardiovascular] disease than if another nucleotide were [was] present at nucleotide position 11 of SEQ ID NO: 5 [the polymorphic site].

20. (Amended) The method of Claim 19, wherein the presence of a thymine [is present] at [the polymorphic site] nucleotide position 11of SEQ ID NO: 5 is indicative of a greater likelihood of the individual's having coronary heart disease.